



EXPRESS MAIL NO. EV335546302US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Orest W. Blaschuk et al  
Application No. : 10/632,678  
Filed : August 1, 2003  
For : COMPOUNDS AND METHODS FOR MODULATING  
CELL ADHESION  
Examiner : Chih-Min Kam, Ph.D.  
Art Unit : 1653  
Docket No. : 100086.401C18  
Date : June 8, 2005

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents:

In accordance with 37 C.F.R. §§ 1.56 and 1.97 through 1.98, applicants wish to make known to the Patent and Trademark Office the references set forth on the attached form PTO-1449. This application is a continuation-in-part and relies, under 35 U.S.C. § 120, on the earlier filing date of prior application USAN 10/464,071, filed June 18, 2003, now pending; which application is a continuation of USAN 09/544,782, filed April 7, 2000, now U.S. Patent 6,610,821; which application is a continuation-in-part of USAN 09/458,870, filed December 10, 1999, now issued as U.S. Pat. No. 6,465,427; which application is a continuation-in-part of USAN 09/357,717, filed July 20, 1999, now issued as U.S. Pat. No. 6,417,325; which application is a continuation-in-part of USAN 09/248,074, filed February 10, 1999, now issued as U.S. Pat. No. 6,346,512; which application is a continuation-in-part of USAN 08/996,679, filed December 23, 1997, now issued as U.S. Pat. No. 6,169,071; which application is a continuation-in-part of USAN 08/893,534, filed July 11, 1997, which application is now issued as U.S. Pat. No. 6,031,072. This application is also a continuation-in-part of USAN 10/359,546, filed February 4, 2003, now U.S. Patent 6,562,786; which application is a continuation of USAN 09/248,015, filed February 10, 1999, now issued as U.S. Pat. No. 6,562,786; which application is

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a continuation-in-part of USAN 08/996,679, filed December 23, 1997, now issued as U.S. Pat. No. 6,169,071; which application is a continuation-in-part of USAN 08/893,534, filed July 11, 1997, now issued as U.S. Pat. No. 6,031,072. The references listed on pages 1-7 of the attached forms PTO-1449 were submitted to and/or cited by the Office in these prior applications and, therefore, are not required to be provided in the present application., Applicants note that copies of the references cited on pages 1-7 of the attached Forms PTO-1449 were also recently submitted to the Patent Office in related application USAN 10/425,557, filed April 28, 2003. However, the references cited on page 8 were not previously made of record, and copies are submitted herewith. If the Examiner wishes, copies of the cited reference will be supplied upon request.

As to any reference cited, applicants do not admit that it is "prior art" under 35 U.S.C. §§ 102 or 103, and specifically reserve the right to traverse or antedate any such reference, as by a showing under 37 C.F.R. § 1.131 or other method. Although the aforesaid references are made known to the Patent and Trademark Office in compliance with applicants' duty to disclose all information they are aware of which is believed relevant to the examination of the above-identified application, applicants believe that their invention is patentable.

Please acknowledge receipt of this Information Disclosure Statement and kindly make the cited references of record in the above-identified application.

A fee of \$180 is submitted in accordance with 37 CFR 1.97(c). The Director is authorized to charge any other fees which may be required, or credit any overpayment to Deposit Account No. 19-1090.

Respectfully submitted,  
Seed Intellectual Property Law Group PLLC



Jeffrey E. Hundley, Ph.D.  
Registration No. 42,676

JEH:ljt/teb

Enclosures:

Forms PTO-1449 (8 Sheets)  
Cited References (8)  
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FORM PTO-1449 (REV.7-80)	U. S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. 100086.401C18	APPLICATION NO. 10/632,678
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		APPLICANTS Orest W. Blaschuk et al.	
		FILING DATE August 1, 2003	GROUP ART UNIT 1653

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AA	5,231,082	07/27/93	Schasteen	514	11	
AB	5,352,667	10/04/94	Lider et al.	514	19	
AC	5,510,628	04/23/96	Georger, Jr. et al.	257	32	
AD	5,585,351	12/17/96	Ranscht	514	12	
AE	5,591,432	01/07/97	Bronson et al.	424	130.1	
AF	5,646,250	07/08/97	Suzuki	530	350	
AG	5,665,590	09/09/97	Yang	435	6	
AH	5,784,294	07/21/98	Platt et al.	364	496	

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION	
				YES	NO
AI	EP 406 428 B1	03/01/95	EPO		
AJ	WO 91/04745	04/18/91	WIPO		
AK	WO 92/08731	05/29/92	WIPO		
AL	WO 94/11401	05/26/94	WIPO		
AM	WO 96/40781	12/19/96	WIPO		

## OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

AN	Alexander et al., "An N-Cadherin-Like Protein Contributes to Solute Barrier Maintenance in Cultured Endothelium," <i>Journal of Cellular Physiology</i> 156: 610-618, 1993.
AO	Ali et al., "Conformationally Constrained Peptides and Semipeptides Derived from RGD as Potent Inhibitors of the Platelet Fibrinogen Receptor and Platelet Aggregation," <i>J. Med. Chem.</i> 37(6): 769-780, 1994.
AP	Beesley, P.W. et al., "The post-synaptic density: putative involvement in synapse stabilization via cadherins and covalent modification by ubiquitination," <i>Biochemical Society Transactions</i> 23(1): 59-64, February 1995.

EXAMINER	DATE CONSIDERED
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\* EXAMINER: Initial if reference considered, whether or not criteria is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant(s).

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	BA	5,939,528	08/17/99	Clardy et al.	530	350	
	BB	6,031,072	02/29/00	Blaschuk et al.	530	317	
	BC	2002/0028453	03/07/02	Keck et al.	435	6	
	BD						

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION
					YES NO
	BE	WO 97/07209	02/27/97	WIPO	
	BF	WO 98/02452	01/22/98	WIPO	
	BG	WO 98/45319	10/15/98	WIPO	
	BH	WO 99/33875	07/08/99	WIPO	
	BI				

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BJ		Blakemore, "Remyelination of CNS axons by Schwann cells transplanted from the sciatic nerve," <i>Nature</i> 266: 68-69, 1977.
BK		Blaschuk et al., "Identification of a Conserved Region Common to Cadherins and Influenza Strain A Hemagglutinins," <i>J. Mol. Biol.</i> 211: 679-682, 1990.
BL		Blaschuk et al., "Identification of a Cadherin Cell Adhesion Recognition Sequence," <i>Developmental Biology</i> 139: 227-229, 1990.
BM		Blaschuk et al., "E-Cadherin, estrogens and cancer: is there a connection?" <i>The Canadian Journal of Oncology</i> 4(4): 291-301, 1994.
BN		Blaschuk and Farookhi, "Estradiol Stimulates Cadherin Expression in Rat Granulosa Cells," <i>Developmental Biology</i> 136: 564-567, 1989.
BO		Blaschuk, O.W. et al., "A Novel Cadherin Antagonist (Exherin) Blocks Human Ovarian Tumor Growth in Nude Mice," <i>Molecular Biology of the Cell</i> 10(Suppl): 72A, November 1999.
BP		Bottenstein and Sato, "Growth of a rat neuroblastoma cell line in serum-free supplemented medium," <i>Proc. Natl. Acad. Sci. USA</i> 76(1): 514-517, 1979.

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CA						

<b>FOREIGN PATENT DOCUMENTS</b>					TRANSLATION
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CB					

**OTHER ART** *(Including Author, Title, Date, Pertinent Pages, Etc.)*

CC	Brecknell et al., "Bridge grafts of Fibroblast Growth Factor-4-Secreting Schwannoma Cells Promote Functional Axonal Regeneration in the Nigrostriatal Pathway of the Adult Rat," <i>Neuroscience</i> 74(3): 775-784, 1996.
CD	Brockes et al., "Studies on Cultured Rat Schwann Cells. I. Establishment of Purified Populations from Cultures of Peripheral Nerve," <i>Brain Research</i> 165: 105-118, 1979.
CE	Brook et al., "Morphology and Migration of Cultured Schwann Cells Transplanted Into the Fimbria and Hippocampus in Adult Rats," <i>GLIA</i> 9: 292-304, 1993.
CF	Byers et al., "Fibroblast Growth Factor Receptors Contain a Conserved HAV Region Common to Cadherins and Influenza Strain A Hemagglutinins: A Role in Protein-Protein Interactions?," <i>Developmental Biology</i> 152: 411-414, 1992.
CG	Cardarelli et al., "The Collagen Receptor $\alpha$ 2 $\beta$ 1, from MG-63 and HT1080 Cells, Interacts with a Cyclic RGD Peptide," <i>The Journal of Biological Chemistry</i> 267(32): 23159-23164, 1992.
CH	Carlstedt et al., "Nerve Fibre Regeneration Across the PNS-CNS Interface at the Root-Spinal Cord Junction," <i>Brain Research Bulletin</i> 22: 93-102, 1989.
CI	Ceppek et al., "Expression of a candidate cadherin in T lymphocytes," <i>Proc. Natl. Acad. Sci. USA</i> 93: 6567-6571, 1996.
CJ	Chuah et al., "Differentiation and survival of rat olfactory epithelial neurons in dissociated cell culture," <i>Brain Research Developmental Brain Research</i> 60: 123-132, 1991.
CK	Craig et al., "Concept and Progress in the Development of RGD-Containing Peptide Pharmaceuticals," <i>Biopolymers (Peptide Science)</i> 37: 157-175, 1995.
CL	Doherty et al., "Neurite Outgrowth in Response to Transfected N-CAM and N-Cadherin Reveals Fundamental Differences in Neuronal Responsiveness to CAMS," <i>Neuron</i> 6: 247-258, 1991.

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**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION
	DB				YES NO

**OTHER ART** *(Including Author, Title, Date, Pertinent Pages, Etc.)*

DC	Doherty and Walsh, "CAM-FGF Receptor Interactions: A Model for Axonal Growth," <i>Molecular and Cellular Neuroscience</i> 8(Article No. 0049): 99-111, 1996.
DD	Doherty and Walsh, "Signal transduction events underlying neurite outgrowth stimulated by cell adhesion molecules," <i>Current Opinion in Neurobiology</i> 4: 49-55, 1994.
DE	Duncan et al., "Transplantation of oligodendrocytes and Schwann cells into the spinal cord of the myelin-deficient rat," <i>Journal of Neurocytology</i> 17: 351-360, 1988.
DF	Fok-Seang et al., "An analysis of astrocytic cell lines with different abilities to promote axon growth," <i>Brain Research</i> 689: 207-223, 1995.
DG	Fok-Seang et al., "Migration of Oligodendrocyte Precursors on Astrocytes and Meningeal Cells," <i>Developmental Biology</i> 171: 1-15, 1995.
DH	Franz, "Percutaneous Absorption. On The Relevance Of In Vitro Data," <i>The Journal of Investigative Dermatology</i> 64(3): 190-195, 1975.
DI	Franz, "The Finite Dose Technique as a Valid <i>in Vitro</i> Model for the Study of Percutaneous Absorption in Man," <i>Curr. Probl. Dermatol.</i> 7: 58-68, 1978.
DJ	Ghirnikar and Eng, "Astrocyte-Schwann Cell Interactions in Culture," <i>GLIA</i> 11: 367-377, 1994.
DK	Gillespie, P. et al., "Conformational Analysis of Dipeptide Mimetics," <i>Biopolymers</i> 43: 191-219, 1997.
DL	Gumbiner et al., "The Role of the Cell Adhesion Molecule Uvomorulin in the Formation and Maintenance of the Epithelial Junctional Complex," <i>The Journal of Cell Biology</i> 107: 1575-1587, 1988.

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	EA						

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					YES NO
	EB				

OTHER ART *(Including Author, Title, Date, Pertinent Pages, Etc.)*

EC	Iruela-Arispe et al., "Expression of SPARC during Development of the Chicken Chorioallantoic Membrane: Evidence for Regulated Proteolysis In Vivo," <i>Molecular Biology of the Cell</i> 6: 327-343, 1995.
ED	Jones, G. et al., "Development of Validation of a Genetic Algorithm for Flexible Docking," <i>Journal of Molecular Biology</i> 267: 727-748, 1997.
EE	Laird et al., "Gap Junction Turnover, Intracellular Trafficking, and Phosphorylation of Connexin43 in Brefeldin A-treated Rat Mammary Tumor Cells," <i>The Journal of Cell Biology</i> 131(5): 1193-1203, 1995.
EF	Leahy, D.J., "Implications of Atomic-Resolution Structures for Cell Adhesion," <i>Annu. Rev. Cell Dev. Biol.</i> 13: 363-393, 1997.
EG	Lee et al., "Expression of the Homotypic Adhesion Molecule E-Cadherin by Immature Murine Thymocytes and Thymic Epithelial Cells," <i>Journal of Immunology</i> 152: 5653-5659, 1994.
EH	Letourneau et al., "Interactions of Schwann Cells with Neurites and with Other Schwann Cells Involve the Calcium-dependent Adhesion Molecule, N-cadherin," <i>Journal of Neurobiology</i> 22(7): 707-720, 1991.
EI	Liuzzi and Lasek, "Astrocytes Block Axonal Regeneration in Mammals by Activating the Physiological Stop Pathway," <i>Science</i> 237: 642-645, 1987.
EJ	Lutz et al., "Secondary Structure of the HAV Peptide Which Regulates Cadherin-Cadherin Interaction," <i>Journal of Biomolecular Structure &amp; Dynamics</i> 13(3): 447-455, 1995.
EK	Matsuzaki et al., "cDNAs of Cell Adhesion Molecules of Different Specificity Induce Changes in Cell Shape and Border Formation in Cultured S180 Cells," <i>The Journal of Cell Biology</i> 110: 1239-1252, 1990.
EL	McCarthy and Vellis, "Preparation of Separate Astroglial and Oligodendroglial Cell Cultures from Rat Cerebral Tissue," <i>J. Cell Biology</i> 85: 890-902, 1980.

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**FOREIGN PATENT DOCUMENTS**

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					YES      NO
	FB				

**OTHER ART** *(Including Author, Title, Date, Pertinent Pages, Etc.)*

FC	Mege et al., "Construction of epithelioid sheets by transfection of mouse sarcoma cells with cDNAs for chicken cell adhesion molecules," <i>Proc. Natl. Acad. Sci. USA</i> 85: 7274-7278, 1988.
FD	Munro et al., "Characterization of Cadherins Expressed by Murine Thymocytes," <i>Cellular Immunology</i> 169(Article No. 0123): 309-312, 1996.
FE	Munro and Blaschuk, <i>Cell Adhesion and Invasion in Cancer Metastasis</i> , R.G. Landes Company, Austin, TX, 1996, Chapter 3, "The Structure, Function and Regulation of Cadherins," pp. 17-34.
FF	Newton et al., "N-Cadherin Mediates Sertoli Cell-Spermatogenic Cell Adhesion," <i>Developmental Dynamics</i> 197: 1-13, 1993.
FG	Nose et al., "Localization of Specificity Determining Sites in Cadherin Cell Adhesion Molecules," <i>Cell</i> 61: 147-155, 1990.
FH	Orr, "Angiogenesis Research Offers New Approaches to Treatment of Disease," <i>Genetic Engineering News</i> , pp. 15-16, 42, May 1, 1996.
FI	Overduin et al., "Solution Structure of the Epithelial Cadherin Domain Responsible for Selective Cell Adhesion," <i>Science</i> 267: 386-389, 1995.
FJ	Redies and Takeichi, "Cadherins in the Developing Central Nervous System: An Adhesive Code for Segmental and Functional Subdivisions," <i>Developmental Biology</i> 180: 413-423, 1996.
FK	Saffell et al., "Expression of a Dominant Negative FGF Receptor Inhibits Axonal Growth and FGF Receptor Phosphorylation Stimulated by CAMs," <i>Neuron</i> , pp. 231-242, February 1997.
FL	Samanen et al., "Development of a Small RGD Peptide Fibrinogen Receptor Antagonist with Potent Antiaggregatory Activity in Vitro," <i>J. Med. Chem.</i> 34(10): 3114-3125, 1991.

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	GA						

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	TRANSLATION
					YES NO
	GB				

OTHER ART *(Including Author, Title, Date, Pertinent Pages, Etc.)*

GC	Sandak, B. et al., "A Method for Biomolecular Structural Recognition and Docking Allowing Conformational Flexibility," <i>Journal of Computational Biology</i> 5(4): 631-654, 1998.
GD	Shapiro et al., "Structural basis of cell-cell adhesion by cadherins," <i>Nature</i> 374: 327-337, 1995.
GE	Starzinski-Powitz, A. et al., "The putative role of cell adhesion molecules in endometriosis: can we learn from tumour metastasis," <i>Molecular Medicine Today</i> 5(7): 304-309, July 1999.
GF	Tsutsui et al., "Expression of Cadherin-Catenin Complexes in Human Leukemia Cell Lines," <i>J. Biochem.</i> 120: 1034-1039, 1996.
GG	Wickelgren, "Breaking the Skin Barrier," <i>PS</i> 12: 86-88, 1996.
GH	Willems et al., "Cadherin-dependent cell aggregation is affected by decapeptide derived from rat extracellular super-oxide dismutase," <i>FEBS Letters</i> 363: 289-292, 1995.
GI	Williams et al., "Activation of the FGF Receptor Underlies Neurite Outgrowth Stimulated by L1, N-CAM, and N-Cadherin," <i>Neuron</i> 13: 583-594, 1994.
GJ	Williams, E. et al., "A Novel Family of Cyclic Peptide Antagonists Suggests That N-cadherin Specificity Is Determined by Amino Acids That Flank the HAV Motif," <i>The Journal of Biological Chemistry</i> 275(6): 4007-4012, February 11, 2000.
GK	Williams et al., "The Primary Structure of Hen Ovotransferrin," <i>Eur. J. Biochem.</i> 122: 297-303, 1982.
GL	
GM	

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	HA						
	HB						

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					YES NO
	HC	WO 98/20897	05/22/98	WIPO	
	HD	WO 99/50281	10/07/99	WIPO	
	HE	WO 01/53331	07/26/01	WIPO	
	HF	WO 01/77146	10/18/01	WIPO	
	HG				

OTHER ART *(Including Author, Title, Date, Pertinent Pages, Etc.)*

HI	Chon, J.H., "Soluble heparin-binding peptides regulate chemokinesis and cell adhesive forces," <i>Am. J. Physiol. Cell Physiol.</i> 280: C1394-C1402, 2001.
HJ	Higashiyama, S. et al., "Heparin-binding EGF-like Growth Factor Stimulation of Smooth Muscle Cell Migration: Dependence on Interactions with Cell Surface Heparan Sulfate," <i>The Journal of Cell Biology</i> 122(4): 933-940, August 1993.
HK	Marutsuka, K. et al., "Protease-activated receptor 2 (PAR2) mediates vascular smooth muscle cell migration induced by tissue factor/factor VIIa complex," <i>Thrombosis Research</i> 107: 271-276, 2002.
HL	Michon, I.N. et al., "The effect of TGF- $\beta$ receptor binding peptides on smooth muscle cells," <i>Biochemical and Biophysical Research Communications</i> 293: 1279-1286, 2002.
HM	

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